There are some relatively large differences between editions in use, so 2005 is blue and 2009 red. Black is valid for both. Sorry for the Czech quotation marks, I forgot to switch languages.

Chapter 4 – meiosis.

Task 1 (p. 28, ed. 2005), Questions and results 1 (p49, ed. 2009)
here is a table from lecture that sums the asnwer up:

	mitosis	**meiosis**
where it happens	all tissues	testis, ovary
what is the result	diploid somatic cell	haploid sperm or egg
DNA replication	1 to 1 division	1 to 2 divisions
prophase length	short, 30 min	long, may last years* * diktyotene
chromosome pairing	no	yes, during „MI“
recombination	rare (repair of breaks)	at least 1 per bivalent necessary
recombination result	gene conversion	crossing over, exchange of chromosome arms
daughter cells	genetically identical	genetically extremely diverse

Task2 (p. 28, ed. 2005), Task 1 (p38, ed. 2009)
a) 2n = 4: 4 types of gametes
b) 2n = 6: 8 types of gametes
c) 2n = 8: 16 types of gametes
c, d) 2^n; human 2^{23} = 8,388,608

Task 3 (p. 28, ed. 2005), Task 2 (p39, ed. 2009)
genotype AaBb, mitosis: daughter cells have always AaBb (except mitotic errors)
genotype AaBb, meiosis: gametes can be of 4 types with equal frequency: AB, Ab, aB, ab (one allele of each gene, see Mendel´s rule of independent segregation, valid for genes on different chromosomes)

Task 4 (p. 29, ed. 2005), Task 3 (p39, ed. 2009)
a) 46 (normal diploid cell)
b) 46 (primary oocytes are entering meiosis [prophase], chromosomes not yet separated)
c) 23 (each has still two sister chromatids)
d) 23 (each has still two sister chromatids)
e) 23 (each has a single chromatid)

Task 5 (p. 29, ed. 2005), Task 4 (p39, ed. 2009)

	molecules	chromosomes	bivalents
pachytene	92	46	23
diplotene	92	46	23
diakinesis	92	46	23
anaphase I	92	46	0
telophase I*	46	23	0
prophase II	46	23	0
metaphase II	46	23	0
telophase II*	23	23	0

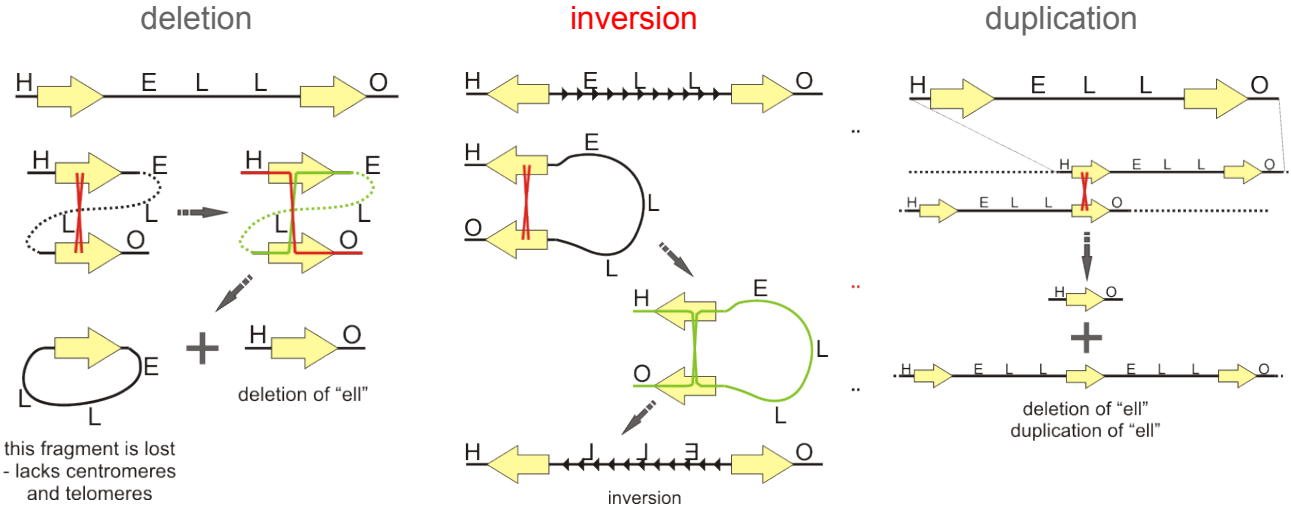
* after cytokinesis, before you should count both sets, like in anaphase

Task 6 (p. 29, ed. 2005)

pachytene

variability goes up (new combinations of existing alleles of different genes)

unequal crossing over can lead to duplication, deletion or inversion. It is usually „provoked“ by sequence similarity of different copies of repeating (repetitive) elements, see this figure (from my lecture, repetitive elements depicted as yellow arrows):



deletions can result from both intrachromosomal (left) and interchromosomal (right) unequal crossing over, inversions require intrachromosomal c.o. (middle), duplication only comes from interchromosomal events (right)

Task 7 (p. 29, ed. 2005), Task 5 (p39, ed. 2009)

independent segregation of each chromosome pair (8,388,608 possibilities for the sperm, the same for the egg)

therefore a couple (man and woman) can have 8,388,608 x 8,388,608 = 70,368,744,177,664 different zygotes

crossing over adds to it different combinations of alleles (haplotypes) for each chromosome. Each crossover doubles the number of possibilities, so if crossovers were fixed and their number would be 40 per pachytene, there will be times 2^{40} for each parent. How to calculate facing the fact that crossovers are not always in the same place is beyond my basic math skills. You can share possible solutions if you have an idea.

Task 8+9 (Task 6+7) roundworms and grasshoppers – look at the pictures

Chapter 5 – human karyotype

Task 2 (p. 78, ed. 2005)
meiosis I X/Y nondisjunction: in all four gemetes there are 92 chromosomes, two gametes are 24,XY and two gametes are 22,0 (normal sperm should be 23,X or 23,Y). All gametes are aberrant (100%). Currently it seems likely that in most cases meiosis I error only affects one chromatid of the tetrad. In such case, there should not be more than 50% aberrant gametes.

Task 3 (p. 78, ed. 2005)
meiosis II X chromosome nondisjunction: two normal gemetes (23,X), one disomic (24,XX) and one nullisomic (22,0). Aberrant gamete frequency 50%.

Task 4 (p. 79, ed. 2005)
meiosis I chromosome 21 nondisjunction: two disomic gametes (24,X,+21) and two nullisomic (22,X,-21)

Task 5 (p. 79, ed. 2005)
meiosis II chromosome 21 nondisjunction: two normal gametes (23,X), one disomic gamete (24,X,+21) and one nullisomic (22,X,-21).

Task 6 (p. 80, ed. 2005), Task 1-4 (p62-63, ed. 2009)
see practical training presentations for the figures

Task 7 (p. 81, ed. 2005), Task 5 (p64, ed. 2009)
a) 0
b) 3
c) 1
d) 4
e) 0
f) 1
g) 1
h) 2
i) 0

Task 8 (p. 81, ed. 2005), Task 6 (p62, ed. 2009)
a) male probably (need to see more cells)
b) female
in 2009 ed.: a) female, b) probably male

Task 9 (p. 82, ed. 2005), Task 7 (p65, ed. 2009)
a+b) 45,X; Turner syndrome. Specifically for a) from the history + physical examination you suspect Turner syndrome and order karyotype examination. However, in addition to 45,X, there can be deletions of only part of X, isochromosome or ring chromosome. There can also be mosaicism (some cells 45,X and some normal 46,XX).
c) no inactivated X
d) see presentations (the text says paternal, which leaves three options: paternal meiosis I, paternal meiosis II X chromosome, paternal meiosis II Y chromosome)

Task 10 (p. 84-5, ed. 2005), Task 8 (p66-7, ed. 2009)
a) Klinefelter syndrome
b) 47,XXY
c) see presentations (text says maternal, which can be mother meiosis I or mother meiosis II)

Task 11 (p. 86, ed. 2005), Task 9 (p68, ed. 2009)

a) at 40 year she has a risk of aneuploidy more than 1%. However, just for the age she seldom sees a geneticist (in this aspect the case story is quite outdated), since the recommended (and taken by majority) procedure is to follow the results of first semester, second semester, or combined screening (ultrasound + mother´s blood parameters) to estimate the risk more thoroughly before refering to a geneticist. Even if she is 40 years, she does not need to go to invasive procedures if the screening is negative. Therefore you can do much less invasive procedures with the same rate of capturing pathological karyotypes. See your protocols for a similar story, but current version with screening.
b) maybe she can undergo at least the second trimester screening now (see sub a), if that was positive, there is a need to get the cells of the baby. In week 16 – amniocentesis.
c) Down syndrome
d) most probably maternal meiosis I error (nondisjunction), picture see presentations

Task 12 (p. 86, ed. 2005), Task 10 (p69, ed. 2009)
In 2005 edition, there is an error, should be 47, XXY not XXXY
color blindness X-linked recessive. Therefore mother X^aX^a, father X^+Y, son X^+X^aY (X^+X^+Y would also have normal vision, but all chromosomes would be from father which is improbable). X^+ and Y are from father – paternal meiosis I.

Task 13 (p. 87, ed. 2005), Task 11 (p69, ed. 2009)
a+b) to complement the list from practical training, I name two more:
DiGeorge syndrome (parathyroid hypoplasia, thymic hypoplasia, and outflow tract defects of the heart), karyotype 46, XX or XY, del22q11.2
Wolf-Hirschhorn syndrome (growth deficiency, dysmorphic head „Greek warrior helmet“ , intelectual disability, epilepsy), 46, XX or XY, del4p16.3
c) Yes, ring chromosomes are often associated with deletions of the subtelomeric regions, usually both p and q. All chromosomes can form a ring chromosome but ring chromosomes are very rare. If the person survives, there can be a lot of abnormalities. These are ascribed to the subtelomeric deletions, not to the ring. Ring 14 and ring 20 are causing epilepsy (among other symptoms), ring X can cause Turner syndrome, like delXp, or i(Xq). It seems a lot of ring chromosome syndromes occur in mosaic state.

Task 14 (p. 87, ed. 2005), Questions and Results 6 (p76, ed. 2009)
a4, b6, c5, d3, e2, f1

Task 15 (p. 87, ed. 2005), Task 12 (p71, ed. 2009)
a) rob(13,21), rob(14,21), rob(15,21), rob(21,21), rob(21,22)
b) in rob(21,21) carrier, there only can be nullisomic gamete and a fused chromosome containing gamete. First leads to lethal monosomy of offspring, second leads to trisomy – rob(21,21), + 21
in other combinations (13-15, 22), the rob chromosome pairs in meiosis I with both remaining normal chromosomes, making a „trivalent“, e.g. 14-rob(14,21)-21. These 3 chromosomes have to split into two gametes, which can be most symetrically done only as 1+2. So for rob(14,21) („rob“ for siplicity), there are 3 possible splittings, making 6 gametes: 14/rob + 21; 21/rob+14; rob/14+21

gametes	14,21	rob	rob,21	14	14,rob	21
zygote	46	45,rob	46,rob,+21	45,-14	46,rob,+14	45,-21
phenotype	normal	normal, balanced	Down	lethal	lethal	lethal

Note that for rob(13,21) there is a risk of both Down and Patau syndromes.
c) no for rob(21,21), yes for other (at least 2/3 of normal babies – counting balanced carrier as normal and not counting the lethal variants)
d) nothing special for rob(21,21) – only egg donation can help. For other, best is probably in vitro fertilization with subsequent karyotyping (usually arrayCGH) of the embryos, normal or balanced embryo is then transferred. Prenatal diagnosis is also possible, but the female may need to „terminate“ some pregnancies before success, which is not a perfect option.

Task 16 (p. 88, ed. 2005), Task 13 (p71-2, ed. 2009)
a+b+c) see solution of Task 15 (Task 12) b)
d) 50%
e) 33%

Task 17 (p. 89, ed. 2005), Task 14 (p73, ed. 2009)
a+b+c) see solution of Task 15 (Task 12) b)
in text questions: 100% Down syndrome in children

Task 18 (p. 90, ed. 2005), Task 15 (p74, ed. 2009)
a) approximately 1:400 (Czech Republic 2015)
b) exponential dependence (risk = constant*exp[maternal age * another constant] + a third constant)
c) mosaicism (with substantial fraction of the aberrant cells, in the preceding table there is a helthy parent with trisomy 21 mosaic, but probably low percentage).
d) „normal" trisomy (nondisjunction of chromosome 21 pair in meiosis I, see first row of the preceding table)
e) empirical risks are lower probably due to spontaneous abortions of a portion of the trisomic fetuses
f) lower empirical risk when father is carrier of balanced translocation – that may be due to more strict chromosome pairing control in spermatocytes vs. oocytes. One piece of evidence is infertility of males and aneuploidy in female offspring in mice deficient for synaptonemal complex protein 3. But I´m far from being convinced that this is 100% explanation.

Task 19 (p. 91, ed. 2005), Questions and Results 5 (p75-6, ed. 2009)
all listed conditions are indications for chromosomal examination

Chapter 6 – gene interactions and multifactorial inheritance.
Section on multifactorial inheritance

Task 1 (p. 92, ed. 2005), keywords and introduction (p81, ed. 2009)
a) additive effect
b) normal distribution N(μ,σ); in the list probably „continuous variation"
c) empirical risk
d) epigenetic. However, in a narrow sense, epigenetic is not in the DNA sequence but still heritable to some extent, this is mechanistically usually DNA methylation or histone modifications.
e) heritability
f) minor gene
g) multifactorial
h) multifactorial treshold model
i) polygenic

Task 2 (p. 93, ed. 2005), Recurrence risk estimates... (p82-3, ed. 2009)
no questions asked

Task 3 (p. 93, ed. 2005), Task 1 (p83, ed. 2009)
a) 200 cm
b) 1:10:45:120:210:252:210:120:45:10:1 (150, 155, 160, ...etc cm). The numbers represent binomial coeficients [n!/k!(n-k)!] with n = number of alleles, k = number of active alleles (1 to n)
c) 160 cm means two active alleles. Then there are 3 possibilities: 1) both active alleles are in one gene in both parents; 2) each active allele is in different gene in each parent; 3) each active allele is in different gene in one parent, but both are in the same gene of the other parent.
For 1) both parent are homozygotes, e.g. AAbbccddee and aabbCCddee. So they can produce only one kind of gametes, i.e. Abcde and abCde, i.e. one active allele, so the offspring would have always 2 active alleles and 160 cm.

2) is more complicated, since both parents are heterozygotes for the genes with active alleles, e.g. AabbCcddee and aaBbccDdee. Therefore each forms 4 kinds of gametes with equal probability: e.g. first parent AbCde, Abcde, abCde and abcde, i.e. 2, 1, 1, and 0 active alleles. The second parent will also produce gametes with 2, 1, 1, and 0 active alleles, so the offspring can be made in a Punnett square like this:

egg\sperm	2	1	1	0
2	4	3	3	2
1	3	2	2	1
1	3	2	2	1
0	2	1	1	0

So it gives 150, 155, 160, 165 and 170 cm with segregation ratio of 1:4:6:4:1.
3) if one parent is homozygote and the second double heterozygote, e.g. AAbbccddee and AabbccDdee, the first is producing only one kind of gametes with 1 active allele, while the second is producing 4 kinds of gametes with 2, 1, 1, and 0 active alleles. So it is like the second or third row of the Punnett square above and there will be 155 (1 active allele, 160 (2 active alleles) and 165 cm (3 active alleles) offspring with the segregation ratio 1:2:1.

Task 4 (p. 93, ed. 2005)
H^2 = genetic variance/all variance = (all variance – environmental variance)/all variance = (F2 variance – F1 variance)/F2 variance = (7.6-1.2)/7.6 = 0.84 (or 84%)

Task 5 (p. 93, ed. 2005), Task 2 (p84, ed. 2009)
AD with penetrance 20% is more likely. With multifactorial traits, the risk is increasing almost in direct proportion with number of affected first degree relatives. However, single AD gene risk is 50% for first, 25% for second and 12.5% for third degree relatives (20% of that gives 10%, 5% and 2.5% risk as stated in the task).

Task 6 (p. 93-94, ed. 2005), Task 3 (p84, ed. 2009)
chromosome X is not transmitted from father to son, while sons of fathers affected with pylorostenosis have more than twice bigger recurrence rate than daughters. So it cannot be X-linked.

Task 7 (p. 94, ed. 2005), Task 4 (p84, ed. 2009)
this can be hard to determine, I see more likely autosomal recessive, since the parents were never affected, which is typical for AR, where in majority of situations parents are heterozygotes. In multifactorial traits, one would expect slightly higer frequency of an affected parent – maybe approximately square root of population frequency incidence of the trait (according to Edward´s formula applied in reverse). Also with decreasing population frequency single gene inheritance is more likely. There can be also higher proportion of consanguinity in parents for AR traits.

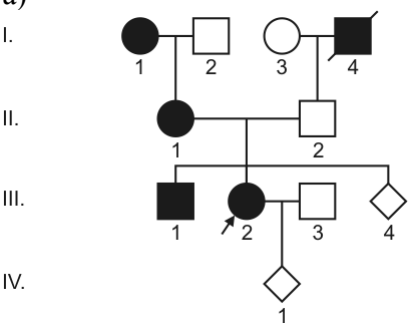
Task 8 (p. 94, ed. 2005), Task 5 (p84, ed. 2009)

	cleft lip	schizophrenia	diabetes mellitus	myopia
population frequency	. 1/900	. 1/100	. 1/16	. 1/10
a) sibs	1/30 (3.3%)	1/10 (10%)	1/4 (25%)	32%
a) offspring	1/30 (3.3%)	1/10 (10%)	1/4 (25%)	32%
b) sibs	2/30 (6.7%)	2/10 (20%)	2/4 (50%)	63%

b) offspring	>1/30 (3.3%)	>1/10 (10%)	>1/4 (25%)	>32%

Task 9 (p. 94, ed. 2005), Task 6 (p85, ed. 2009)
a) sqrt(0.0009) = 0.03 (3%)
b) 3%
c) another sib of the proband 6%, a child of the proband >3%

Task 10 (p. 94, ed. 2005), Task 8 (p85, ed. 2009)
a)



b) sqrt(0.16) = 0.4 (40%) - risk for the child >40%, risk for another sib =3x40% … 100%

Yellow labeled parts of task 8, 9 and 10 (ed. 2005): The disease is present in both first and second degree relatives. There is an Edward´s formula for second and third degree relatives: risk2nd = (population incidence)$^{3/4}$, risk3nd = (population incidence)$^{7/8}$. However, as Ian D. Young writes in „Introduction to risk calculation in genetic counselling“, Oxford University Press 2007, if you sum the risks up, you may underestimate the real risk. Empirical risk tables are then much better. Nevertheless, if nothing better is available, we do the summation:

In task 8b: If proband and one of his parents is affected, the child of the proband has one first and one second degree relative. Risk = (population incidence)$^{1/2}$ + (population incidence)$^{3/4}$ numerically:

	cleft lip	schizophrenia	diabetes mellitus	myopia
	3.9%	13.2%	37.5%	49.4%

In task 9c: same calculation as above in 8b, risk = 3.5%

In task 10b: risk for proband´s child - if we sum the risk from one first, two second and two third-degree relative, we get cca 130%. That is nonsense, even 100% is improbable (not all children must be allergic). So the risk is probably overestimated. The reason is likely due to limitations of Edward´s formula, which is working well for low population incidence, up to 1%, and relatively high heritability, cca 80%. Allergy has much higher incidence, heritability estimates can be as low as 35% (but some claim up to 84%).

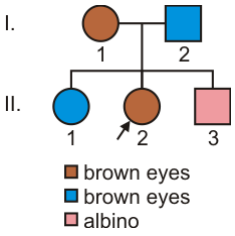
Section on gene interactions
Task 1 (p. 95, ed. 2005), Task 1 (p77-8, ed. 2009)
F1 genotype: CcBb
F1 phenotype: black
F1 gametes: CB, Cb, cB, cb
F2 genotypes:

	CB	Cb	cB	cb
CB	CCBB	CCBb	CcBB	CcBb

Cb	CCBb	CCbb	CcBb	Ccbb
cB	CcBB	CcBb	ccBB	ccBb
cb	CcBb	Ccbb	ccBb	ccbb

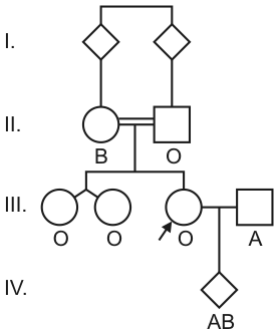
F2 phenotypes: 9 black : 3 brown : 4 albino (albino are all „cc“, brown are all „bb“ with at least one „C“.
type of interaction: recessive epistasis

Task 2 (p. 96, ed. 2005), Task 2 (p78, ed. 2009)



mother CcBb, father Ccbb, first daughter C-bb, second daughter C-Bb, son cc-b.
a) 25% albino
b) =0,75*0,5 = 0,375 => 37,5% brown eyed
c) 37,5% blue eyed

Task 3 (p. 96, ed. 2005), Task 3 (p79, ed. 2009)
chart:



genotypes: mother (I set her proband) hhBO, father (probably) HHAO/HHAA, child HhAB, grandmother HhBB/HhBO, grandfather HhOO, twin sisters hhBO/hhOO
type of interaction: recessive epistasis

Task 4 (p. 96-7, ed. 2005), Task 4 (p80-81, ed. 2009)
a) 9/16 = 0,5625
b) recessive epistasis

Task 5 (p. 97, ed. 2005), Task 5 (p81, ed. 2009)
a) DdEe; all children hearing
b) DDEE, DdEE, DDEe, DdEe; all children hearing
c) better draw Punnett rectangle:

	DE	dE
DE	DDEE	DdEE
De	DDEe	DdEe
dE	DdEE	ddEE

de	DdEe	ddEe

However, there is no risk for gene E, only for gene D – 25% children not hearing
d) equivalent to the situation sub c), just the genes are switched – there is 25% risk coming from gene E.
type of interaction: complementarity

Task 6 (p. 98, ed. 2005), Questions and Results 4 (p86, ed. 2009)
genetic heterogeneity

Task 7 (p. 98, ed. 2005)
a) both are probably autosomal recessive
b) complementarity (mother AAbb, father aaBB, children AaBb)
c) not more than population risk (i.e. very low)
d) almost 100%